1. An optical system for *in vivo*, non-invasive imaging of tissue change comprising:

an optical module including an array of input ports and detection ports located in a selected geometrical pattern to provide a multiplicity of arrayed single source, single detector pairs enaged directly with the subject;

a spectrophotometer including

light source means constructed to introduce electromagnetic radiation of visible or infra-red wavelength into the examined tissue successively at said input ports, said wavelength being sensitive to a constituent of the imaged tissue; detector means constructed to detect, at said detection ports, radiation of said selected wavelength that has migrated in the tissue from respective input ports; and

a processor receiving signals of said detected radiation from said detector means, and constructed and arranged to create a defined spatial image of the tissue by effectively producing from signals from the multiplicity of arrayed single source, single detector pairs, a succession of data sets representing, from a selected view, a succession of spatial images of the tissue, and an image data set related to differences between data of said successive data sets.

2. An optical system for *in vivo*, non-invasive functional neuroimaging of tissue comprising:

a stimulator constructed to stimulate a selected functional activity of neural tissue of interest;

an optical module including an array of input ports and detection ports located in a selected geometrical pattern to provide a multiplicity of arrayed single source, single detector pairs engaged directly with the subject;

a spectrophotometer including

light source means constructed to introduce electromagnetic radiation of visible or infra-red wavelength into the examined neural tissue successively at the input ports, the wavelength being sensitive to a tissue constituent associated with a physiological response of the imaged functional activity;

detector means constructed to detect, at said detection ports, radiation of the selected wavelength that has migrated in the stimulated neural tissue from respective input ports; and

a processor receiving signals of said detected radiation from said detector means, and constructed and arranged to create a defined spatial image of the functional activity of neural tissue by effectively producing from the signals from the multiplicity of arrayed single source, single detector pairs, a first data set representing, from a selected view, a spatial image of the neural tissue at rest, a second data set representing, from the same selected view, a spatial image of the neural tissue during stimulation, and a functional image data set that is related to the differences between said first and second data sets, over said sets.

3. The optical system of claim 1 or 2 wherein said optical module is constructed to maintain a selected distance between said input and detection ports for the respective source-detector pairs during the production of said first and second data sets, said distance being selected according to the tissue depth desired to be imaged.

4. The optical system of claim 1 or 2 in which said optical module or an associated set of said modules is constructed to take readings at different depths to produce 3D data sets from which an image data set may be produced.

5. The optical system of claim 1 or 2 in which said processor is adapted to produce said image data set by implementing an optical tomography algorithm.

6. The optical system of claim 5 in which said optical tomography algorithm employs factors related to determined probability distribution of photons attributable to the scattering character of the tissue being imaged.

7. The optical system of claim 1 or 2 constructed to form said image data set from a part of the head.

8. The optical system of claim 7 constructed to form said functional image data set from below the surface region of the cortex.

9. The optical system of claim 2 wherein said stimulator is constructed to stimulate the visual cortex.

10. The optical system of claim 2 wherein said stimulator is constructed to stimulate the cognitive cortex.

11. The optical system of claim 2 wherein said stimulator is constructed to stimulate the sensory motor cortex.

12. The optical system of claim 2 wherein said stimulator is constructed to stimulate spinal tissue.

13. The optical system of claim 2 wherein said stimulator is constructed to deliver electrical signals to selected tissue.

14. The optical system of claim 2 wherein said stimulator is constructed to apply an electrical field to selected tissue.

15. The optical system of claim 2 wherein said stimulator is constructed to deliver magnetic signals to selected tissue.

16. The optical system of claim 1 or 2 wherein said image set is related to at least one of the group consisting of blood volume, hemoglobin oxygenation or deoxygenation, photon absorption coefficient, photon scattering coefficient, refractive index, change in magnetic field, change in electric field, production of or change of a specific tissue constituent, and production of or change in the concentration of a pigment.

17. The optical system of claim 1 or 2 wherein said tissue constituent is an endogenous pigment.

18. The optical system of claim 1 or 2 wherein said endogenous pigment is hemoglobin.

19. The optical system of claim 1 or 2 wherein said tissue constituent in an exogenous pigment.

20. The optical system of claim 19 in which said exogenous pigment is a selected contrast agent.

21. The optical system of claim 1 or 2 in which the source means, the detector means, the source to detector distance, and the rate of excitation and detection are selected to enable said image data set to be obtained within a short time.

22. The optical system of claim 1 or 2 wherein said spectrophotometer further includes

a first oscillator constructed to generate a first carrier waveform at a first frequency on the order of 10^8Hz, said first frequency having a time characteristic compatible with the time delay of photon migration from an input port to a detection port in the examined tissue;

said light source means being coupled to said first oscillator and constructed to generate said radiation modulated by said first carrier waveform;

a phase detector constructed to determine change in waveform of the detected radiation relative to the waveform of the introduced radiation and measure therefrom the phase shift of said detected radiation at said wavelength, said phase-shifted radiation being indicative of scattering or absorptive properties of the examined tissue; and

said processor constructed to create said image data set based at least in part on the measured phase shift.

23. The optical system of claim 22 further comprising

a second oscillator constructed to generate a second waveform at a second frequency;

said detector means arranged to receive a reference waveform at a reference frequency offset by a frequency on the order of 10^3Hz from said first frequency and to produce a signal, at said offset frequency, corresponding to said detected radiation; and

said phase detector adapted to compare, at said offset frequency, the detected radiation with the introduced radiation and to determine therefrom the phase shift at said wavelength.

24. The optical system of claim 1 wherein said spectrophotometer includes

a light source, means constructed to generate pulses of radiation of said wavelength, said pulses having duration on the order of a nanosecond or less;

said detector means being constructed to detect over time photons of modified pulses that have migrated in the tissue from said input ports;

an analyzer, connected to said detector means, adapted to determine a change in the pulse waveform shape of said detected pulses relative to said introduced pulses, at said wavelength; and

said processor being constructed and arranged to create said image data set based on said determined pulse waveform change.

25. The optical system of claim 24 wherein said processor is constructed and arranged to calculate the effective pathlength of photons of said wavelength migrating between said input and detection ports in conjunction with creating said image data set.

26. The optical system of claim 24 wherein said processor is constructed and arranged to calculate the scattering coefficient at said wavelength in conjunction with creating said image data set.

27. The optical system of claim 24 wherein said processor is constructed and arranged to calculate the absorption coefficient at said wavelength in conjunction with creating said image data set.

28. The optical system of claim 1 or 2 constructed to introduce and detect photons at two wavelengths selected to provide sensitivity to a property of said constituent.

29. The optical system of claim 1 or 2 in which said source means comprises one or more incandescent lamps.

30. The optical system of claim 1 or 2 in which said source means comprises one or more photo diodes.

31. An instrument for functional imaging of brain activity of a subject comprising a brain imager, including an array of sources and detectors defining a multiplicity of source-detector pairs, constructed and arranged to image hemoglobin, deoxyhemoglobin or blood volume at depth within the brain during administration of a respective stimulus to the subject, said brain imager including

a processor receiving signals of said detected radiation from said detector, and constructed and arranged to create a defined spatial image of the functional activity of neural tissue by effectively producing a first data set representing, from a selected view, a spatial image of blood in the cortex while the subject is at rest, a second data set representing, from the same selected view, a spatial image of the blood in the cortex during stimulation, and a functional image data set that is related to the differences between said first and second data sets, over said sets.

32. The device of claim 31 in the form of a near infrared hemoglobinometer based on introducing and detecting photons that have migrated through tissue of the head.

33. The device of claim 32 having multiple source-detector pairs for engaging the skull, the source being spaced from the detector for selected pairs between about 1.5 and 7 cm.

34. The device of claim 33 in which the spacing is 2.5 cm or greater.

35. The device of claim 31 having a multiplicity of light sources and detectors defining an array of source-detector pairs, and

a control for energizing one source at a time enabling accumulation of single source-detector responses.

36. The device of claims 31, 32 or 33 in which the light source or sources are incandescent lamps.

37. The instrument of claim 32 comprising

an array of sources of near infrared or visible photons,

an array of detectors positioned to receive photons from the sources in respective source-detector pairs following migration of the photons from the sources through the tissue,

a system enabling numerous readings of migrated photons to be taken systematically at the detectors for different source-detector positions relative to the tissue, and

a processor employing an imaging algorithm based on respectively different probabilities for a given source-detector position, for photons from the source passing through different regions of the volume of the scattering tissue that are located at different positions distributed laterally from a straight reference line between source and detector.

38. An instrument for functional imaging of brain activity of a subject comprising an imager constructed and arranged to image hemoglobin, deoxyhemoglobin or blood volume, said imager comprising

an array of sources of near infrared or visible photons,

an array of detectors positioned to receive photons from the sources following migration of photons from the sources through the tissue,

a system enabling numerous readings of migrated photons to be taken systematically for different source-detector positions relative to the tissue, and

a processor employing data sets taken during rest and during stimulation, with an imaging algorithm that is based on respectively different probabilities for a given source-detector position, for photons from the source passing through different regions of the volume of the scattering tissue that are located at different positions distributed laterally from a straight reference line between source and detector.

39. The imaging instrument of claim 37 or 38 in which the imaging algorithm is a back-projection algorithm, and said probabilities are implemented as respectively different weight factors employed in the algorithm for detected energy for different pixels of the image.

40. The instrument of claim 31, 37 or 38 constructed to store at least one set of data for a given area of the brain while the subject is at rest and at least one set of data for the given area of the brain while the subject is stimulated, and to produce a defined output image representing the differences over the area of the respective sets of data.

41. The imaging instrument of claim 1, 37 or 38 in which the light sources produce relatively long light pulses and the instrument functions according to continuous wave spectroscopy.

42. The imaging instrument of claim 41 constructed to take and employ readings at least at two different wavelengths.

43. The imaging instrument of any of the claims 1, 37 or 38 in which an incandescent lamp is provided to produce the photons introduced at the sources.

44. The imaging instrument of claim 43 in which an array of miniature incandescent lamps is arranged to be sequentially illuminated.

45. The imaging instrument of claim 1, 2, 31, 37, or 38 in which each source is laterally displaced from its detector or detectors on the surface of a subject at a side by side spacing between about 1.5 and 7 cm to establish a banana-shaped probability gradient of migrating photons in the tissue that extends from source to detector.

46. A method of producing an image from a volume of light-scattering tissue of a living subject comprising,

providing and employing on the subject an imaging instrument according to claim 1, 37 or 38.

47. The method of claim 46 including introducing an optical contrast agent or a drug to the blood stream of the subject, and

producing with the instrument an image data set for the tissue while the contrast agent or drug is present in blood circulating in the tissue of the subject or is present in the localized tissue.

48. An optical system for *in vivo*, non-invasive imaging of biological tissue comprising:

a stimulator constructed and arranged to stimulate cognition in a subject;

a spectrophotometer co-operatively arranged with said stimulator;

an optical module constructed to provide a multiplicity of arrayed source-detector pairs constructed for direct engagement with the subject;

a light source constructed to introduce electromagnetic radiation of a visible or infra-red wavelength into biological tissue;

a light detector constructed to detect optical radiation that has migrated in the tissue; and

a processor coupled to receive signals of said detected radiation from said light detector, and constructed and arranged to create a defined spatial image of the tissue by effectively producing image data corresponding to differences between two data sets of the tissue being stimulated and the tissue not being stimulated by said stimulator.

49. The optical system of claim 48 wherein said optical module is constructed to prevent migration of superficial photons migrating on a tissue surface.

50. The optical system of claim 48 wherein said optical module is constructed to be positioned on the exterior surface

of the head and also constructed to prevent migration of superficial photons migrating on a tissue surface.

51. The optical system of claim 48 wherein said optical module including said arrayed source-detector pairs are constructed to include one said light detector located symmetrically with respect to several said light sources for providing the respective source-detector pairs.

52. The optical system of claim 48 wherein said optical module is constructed to maintain a selected distance between said source-detector pairs during the production of said data sets, said distance being selected according to the tissue depth desired to be imaged.

53. The optical system of claim 52 wherein said processor is constructed to produce 2D data for said tissue depth.

54. The optical system of claim 52 wherein said processor is constructed to produce 3D data sets from which said image data set, related to said differences, is produced.

55. The optical system of claim 48 wherein said processor calculates said image data set by implementing an optical tomography algorithm.

56. The optical system of claim 55 wherein said optical tomography algorithm employs factors related to determined probability distribution of photons attributable to the scattering character of the tissue being imaged.

57. The optical system of claim 48 wherein said optical module including said arrayed source-detector pairs are constructed for imaging of frontal tissue of the head.

58. The optical system of claim 48 wherein said optical module including said arrayed source-detector pairs form a symmetrical pattern.

59. The optical system of claim 48 wherein said image set is created from data related to at least one of the group consisting of: blood volume, hemoglobin oxygenation, hemoglobin deoxygenation, photon absorption coefficient, photon scattering coefficient, and refractive index.

60. The optical system of claim 48 including optical fibers for coupling light between the examined tissue and said light source and detector.

61. The optical system of claim 48 in which each source is laterally displaced from said respective detector on the surface of a subject at a side by side spacing between about 1.5 and 7 cm to establish a banana-shaped probability distribution of migrating photons in the examined tissue.

62. An instrument for functional imaging of brain activity of a subject, comprising

a stimulator constructed and arranged to stimulate a cognitive activity; and

an imager constructed and arranged to image optical data related to hemoglobin, deoxyhemoglobin or blood volume, said imager comprising

an array of sources for emitting a near infrared or visible wavelength into brain tissue,

an array of detectors positioned to receive photons of said wavelength that have migrated from the sources inside the tissue,

a system enabling numerous readings of migrated photons to be taken systematically for different source-detector positions relative to the tissue, and

a processor employing data sets taken to create a defined spatial image of the tissue using multiplicity of arrayed source-detector pairs providing optical signal of the tissue being stimulated and the tissue not being stimulated by said stimulator.

63. A method of *in vivo*, non-invasive imaging of tissue change related to cognition, comprising:

providing a stimulator constructed and arranged to stimulate a cognitive activity of a subject;

providing an array of input locations and detection locations arranged over a selected geometrical pattern to provide a multiplicity of photon migration paths in brain tissue,

introducing electromagnetic radiation of a visible or infra-red wavelength into the brain tissue selectively at said input locations, said wavelength being sensitive to a constituent of the tissue;

detecting, at said detection locations, radiation of said selected wavelength that has migrated in the tissue from at least one input location;

stimulating a cognitive activity of the subject;

repeating said introduction and detection while stimulating said cognitive process;

and

creating a defined spatial image of the tissue based on signals from said multiplicity of said photon migration paths detected for brain tissue being stimulated and brain tissue not being stimulated.

64. The imaging method of claim 63 including detecting radiation for a selected input and detection separation to produce 2D data sets.

65. The imaging method of claim 63 including detecting radiation for different input and detection separation to produce 3D data sets.

66. The imaging method of claim 63 further including calculating said image related to at least one of the group consisting of: blood volume, hemoglobin oxygenation, hemoglobin deoxygenation.

67. The imaging method of claim 63 further employing a second wavelength.

68. The imaging method of claim 63 further including introducing an optical contrast agent to the blood stream of the subject, and

producing said image data sets for the tissue while the contrast agent is present in the blood circulating in the tissue of the subject.

69. The imaging method of claim 63 further including introducing a drug to the blood stream of the subject, and

producing said image data sets for the tissue while the drug is present in the blood circulating in the tissue of the subject.

70. The imaging method of claim 63 wherein said stimulating includes displaying words to the subject.

71. The imaging method of claim 63 wherein said stimulating includes displaying words to the subject for the purpose of translating said displayed words from one language to another.

72. The imaging method of claim 63 wherein said stimulating includes providing signals for the subject to displace a body part.

73. The imaging method of claim 63 wherein said stimulating includes providing signals for the subject for initiating finger tapping.

74. The imaging method of claim 64 wherein said imaging includes imaging the cognitive activity in the prefrontal cortex of the subject.

75. The imaging method of claim 74 wherein said stimulating includes displaying words to the subject for the purpose of translating said displayed words from one language to another.

76. The imaging method of claim 74 wherein said creating said defined spatial image includes calculating a blood volume.

77. The imaging method of claim 74 wherein said creating said defined spatial image includes calculating hemoglobin oxygenation.

78. The imaging method of claim 74 wherein said creating said defined spatial image includes calculating hemoglobin deoxygenation.

79. The instrument of claim 62 wherein said stimulator includes a display.

80. The instrument of claim 79 wherein said display is constructed to display words to a subject.

81. The instrument of claim 62 wherein said stimulator is constructed to generate sound.

82. The instrument of claim 62 wherein said stimulator is constructed to generate vibrations.

83. The instrument of claim 79 wherein said imager is constructed to image the cognitive activity in the prefrontal cortex of the subject.

84. The instrument of claim 62 wherein said processor is constructed to calculate a blood volume.

85. The instrument of claim 62 wherein said processor is constructed to calculate hemoglobin oxygenation.

86. The instrument of claim 62 wherein said processor is constructed to calculate hemoglobin deoxygenation.